IN brief

TNF-α blockers and tumors

A Danish study has found no increase in cancer risk in people taking tumor necrosis factor alpha (TNF-α) inhibitors over a long period. The authors (*Ann. Rheum. Dis.* **70** (suppl. 3), 410, 2011) cross-referenced data from 5,598 patients included in DANBIO, the national Danish Rheumatological registry set up in 2000 to monitor individuals treated with biologic drugs, with the Danish Cancer Registry. They concluded that, "No overall or specific elevation of cancer risk was observed during up to nine years of follow-up." The cohort, mainly treated for rheumatoid arthritis with TNF-α blockers Humira (adalimumab), Remicade (infliximab) and Enbrel (etanercept) from 2000 to 2008, will continue to be followed. Given the cytokine's role in immune surveillance for cancer, it was always anticipated that blocking anti-TNF-α might leave patients open to a higher risk of malignancies. This led to black box warnings and, in August 2009, the US Food and Drug Administration (FDA) added specific information about the risk of lymphomas and other rare cancers in pediatric patients. But the overall level of risk remains unclear. As recently as December 2010, a meta-analysis, commissioned by the European Medicines Agency, of 74 randomized controlled trials involving 15,418 patients treated with TNF-α blockers, could neither "refute nor verify" any link. The recent results do not mean TNF-α blockers are in the clear yet. Lead author Lene Dreyer of the Department of Rheumatology at Gentofte University Hospital in Denmark said, "Drugs targeting TNF can influence the development of tumors, although the extent of this impact remains unclear." *Nuala Moran*

Swiss food giant enters diagnostics

Nestle's buyout of San Diego–based Prometheus Laboratories marks a strategic shift by the Vevey, Switzerland–based food company into personalized medicine. Prometheus is a specialty pharma and diagnostics firm, focused on gastroenterology and oncology services to guide the use of targeted therapies. The financial terms were not disclosed, though the transaction is estimated at over $1.1 billion, and is being conducted by Nestle Health Science, a subsidiary formed in January to specialize in health nutrition. "I know there's not any other food company in the world that has created a division specifically to explore and exploit the overlap between pharmaceuticals and food," says independent food industry consultant, James Amoroso, of Walchwil, Switzerland. By adding Prometheus, Nestle acquires a Crohn's disease prognostic test and a diagnostic for inflammatory bowel disease among others. It also pulls in rights to cancer drugs Proleukin, originated by Novartis of Basel, and Rencarex (girentuximab), a targeted antibody for targeting solid tumors licensed from Munich-based Wilex. Also recently, Nestle added nutritional products manufacturers Vitaflo of Liverpool, UK, and CM&D Pharma, of Munich. Nestle spent $1.9 billion on R&D in 2010. "They've got enough pure research going on, as well as applied research," Amoroso says, "that they know there are areas to exploit." *Karen Carey*

US court bolsters biotech patent protection

On May 23, the US Court of Appeals for the Federal Circuit's (CAFC) ruling in *Therasense vs. Becton Dickinson & Company* raised the standards for charging inequitable conduct. This is good news for biotech companies, as the ruling will likely stem inequitable conduct charges, a litigation tactic often used by patent infringers to render an innovator's patent unenforceable or to delay settlement.

"It has become almost routine to assert [the inequitable conduct] defense in litigation," says Courtenay Brinckerhoff, partner with Foley & Lardner, Washington, DC, and vice chair of the firm's chemical, biotech & pharma practice. Indeed, CAFC described the practice as a "plague" on the patent system. The more stringent standards for proving inequitable conduct should now embolden innovator companies to pursue licensing agreements and enforce patents and might also bring down their costs in litigating against patent infringers.

The inequitable conduct defense centers on proving that a patent holder failed to disclose all material information to the US Patent and Trademark Office (USPTO) at the time of filing, thus violating its duty to the USPTO. The consequences of being found guilty of inequitable conduct falls on patent owners, which can create serious problems. "Being found guilty of inequitable conduct carries a harsh penalty—namely unenforceability of the entire patent—[a possibility] that can cast a long shadow over a patent," says Brinckerhoff.

Inequitable conduct stems from a principle referred to as 'unclean hands' established in the 1930s and 1940s, during three US Supreme Court cases. The Court held that perjury and the manufacture of false evidence to mislead the USPTO constituted inequitable conduct. Over the years, the elements proliferated and expanded to include nondisclosure of information to the USPTO. This includes failing to submit items such as references, papers or abstracts from conferences as prior art (that is, information in the public domain that could be relevant to determining if the invention described in the patent is novel).

To prove a patentee is guilty of inequitable conduct, two criteria must be met: intent to deceive the USPTO and a determination of whether the information that was withheld was material (that is, important to the issuing of the patent). The stringency for meeting these criteria has relaxed in recent years; so much so that inequitable conduct has been gaining popularity as a litigation defense tactic.

In the *Therasense* case (http://www.cafc.uscourts.gov/images/stories/opinions-orders/08-1511.pdf), the CAFC realized lowered standards had led to increasing misuse of the inequitable conduct charge during litigation, so it revisited its definition of nondisclosure of information. According to CAFC's new definition, the charge of omitting prior art references can only be leveled against a patentee if it can be determined that, had the USPTO

The US Court of Appeals for the Federal Circuit's recent ruling on inequitable conduct is viewed as positive for biotech.